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## PULMONARY CRYPTOCOCCOSIS IN AIDS PATIENTS : RADIOGRAPHIC APPEARANCES AND SOME CLINICAL ASPECTS

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### ABSTRACT

**PURPOSES :** To study radiographic appearances and some clinical aspects of pulmonary cryptococcosis in AIDS patients.

**MATERIALS AND METHODS :** Medical records and chest radiographs were retrospectively reviewed during October 1990 to February 1996

**RESULTS ;** Pulmonary cryptococcosis were diagnosed in 22 patients with AIDS (21 men, 1 woman ; age range 22-64 years). Fever, cough, headache and dyspnea were the main presenting symptoms. The most common radiographic appearance was diffusely mixed interstitial infiltration, predominantly fine or intermediate pattern (12/22). Bilateral coarse interstitial infiltration were noted in 2 patients, localized infiltration in 6 patients, unilateral pleural effusion with questionable infiltration in 1 patient and mediastinal adenopathy alone in 1 patient. Associated minimal pleural effusion and cavities were found as associated lesions in 5 and 2 patients respectively. Seventeen patients had concurrent cryptococcal meningitis with or without cryptococcal infection of other organs and 2 patients had cryptococemia. Four cases could be diagnosed as pulmonary cryptococcosis prior to cryptococcal meningitis. Of the 18 patients receiving antifungal drugs, 13 patients improved and 5 patients died. The remaining 4 patients who had no specific treatment were all dead.

Pulmonary cryptococcosis should be the considered diagnosis more frequently in AIDS patients. In the presence of cryptococcal meningitis with abnormal chest radiograph, the earlier it was diagnosed, the better will be the treatment outcome.

Cryptococcal neoformans infection at the present time has been an important problem accompanying world-wide spread of the HIV virus. It is the fourth most common systemic opportunistic infection in patients with AIDS in USA<sup>1</sup> whereas it is the second most common in Thailand following tuberculosis.<sup>2</sup> The organisms usually infect meninges and brain but many other organs could also be involved particularly the lung.<sup>3</sup> The prevalence of pulmonary cryptococcosis is expected to increase. Hence the purposes of this study are to describe radiographic appearance of pulmonary cryptococcosis in comparison with others and to describe some aspects of clinical manifestations.

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## MATERIALS AND METHODS

Medical records and chest radiographs of patients with AIDS and pulmonary cryptococcosis diagnosed during October 1990 to February 1996 in Bamrasnaradura Hospital were retrospectively reviewed. The pulmonary cryptococcosis was definitely diagnosed by the presence of organism in histopathologic specimen (from either biopsy or necropsy material) or probably diagnosed by the presence of organism on stain and/or culture of bronchial secretion or fluid with correlated chest radiograph. We excluded patient who has other coexisting pathogen in the lung.

Chest radiographs were independently analysed by 4 radiologists from Bamrasnaradura Hospital and Central Chest Hospital. The following were recorded: presence or absence of infiltration, any ground-glass appearance, cavity, pleural effusion and lymphadenopathy. Types of infiltration were classified as predominantly alveolar or interstitial pattern which was also divided to be fine or intermediate or coarse interstitial pattern. If there was any different radiographic interpretation the consensus would be needed for final opinion.

## RESULTS

There were 22 AIDS patients with documented pulmonary cryptococcosis. Twenty-one patients were men and 1 was woman with ages

ranging from 22 to 64 years. Twelve patients were heterosexual, 2 were homosexual and intravenous drug users, 2 were bisexual and 6 had no documented risk factor. Most of the patients presented with fever, cough and headache. (Table.1) Four patients had lung crepitation and only 5 patients had obvious neck stiffness on physical examination. The duration of symptoms varied from 1 week in 5 patients, around 1 month in 11 patients and 2-4 months in 6 patients.

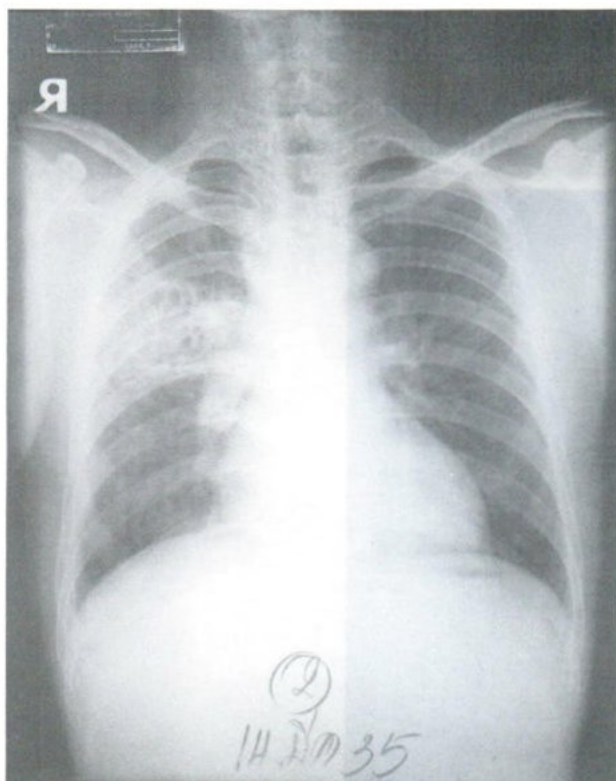
Eight patients met criteria of definite diagnosis for pulmonary cryptococcosis and the remaining 14 patients met criteria of probable diagnosis.

Diffuse infiltration in both lungs, predominantly interstitial pattern were presented in 14 patients, localized infiltration in 6 patients (Fig.1) and mediastinal adenopathy without infiltration was seen in only 1 patient (Fig.2). One patient had mild to moderate degree of Rt. pleural effusion with equivocal infiltration or crowded interstitial markings in Rt lung. (Table 2) Of the 14 patients with diffuse infiltration ; 7 were fine pattern (Fig.3), 2 were coarse pattern (Fig. 4) and 5 were intermediate pattern. Ground- glass patterns were described in 4 of 14 patients with diffuse infiltration. (Fig. 5) Most of diffuse infiltration pattern involved the mid or the lower lung zones more than the upper zone.

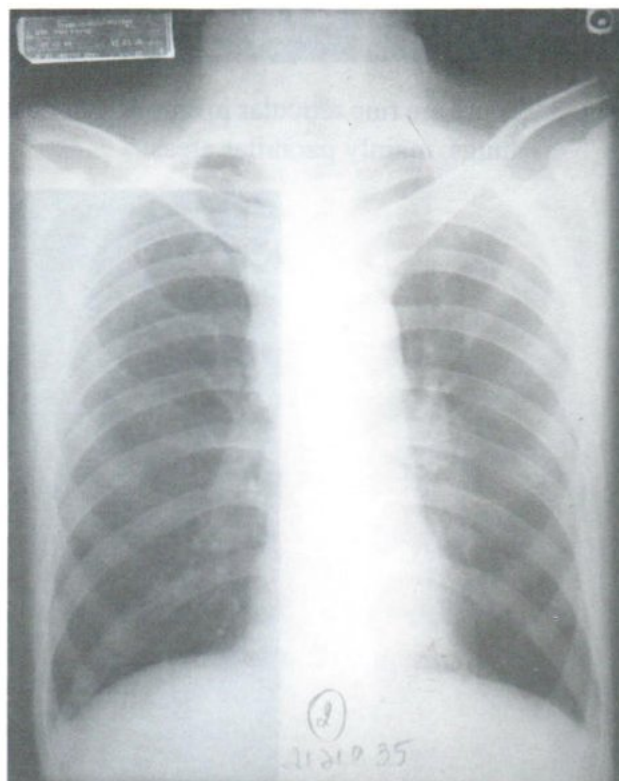


**Table 1.** Summaries of symptoms and signs of 22 AIDS patients with pulmonary cryptococcosis

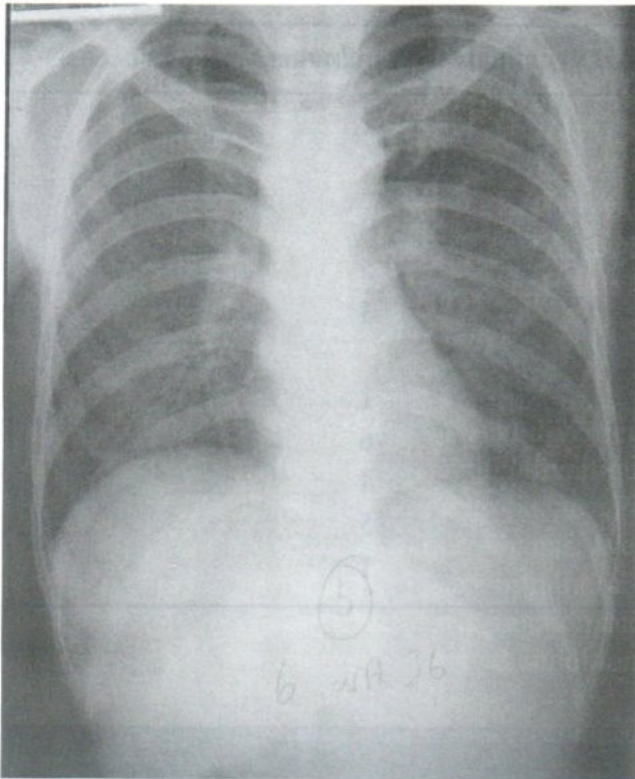
fever	17
cough	12
headache	9
dyspnea	5
gastrointestinal symptoms (diarrhea,nausea,vomitting,melena)	3
chest pain	1
adenopathy	6
lung crepitations	4
neck stiffness	5
skin nodules	1



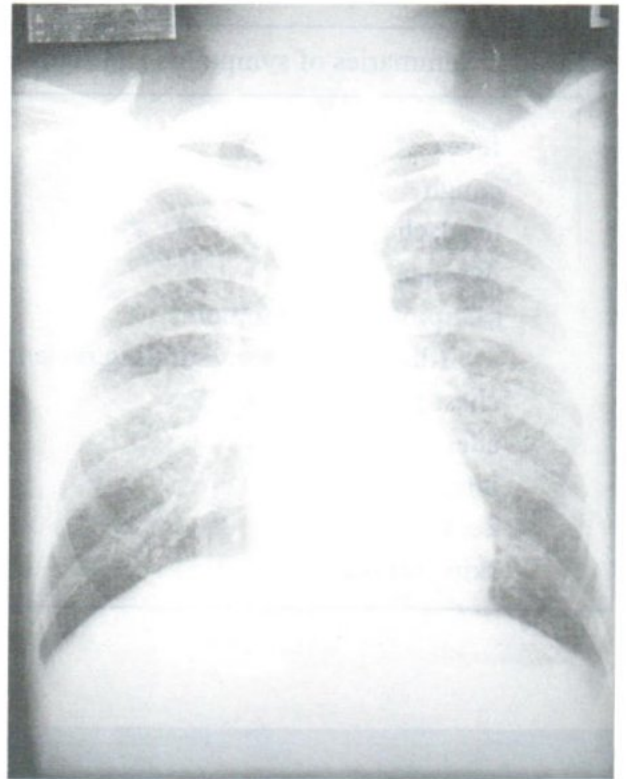
**Fig. 1** Localized infiltration are present in Rt. upper lobe.



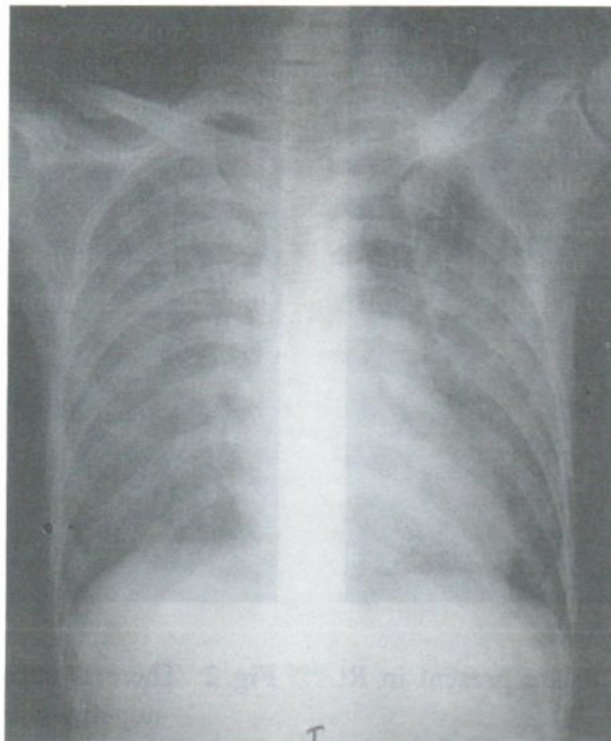
**Fig. 2** There is superior mediastinal lymphadenopathy without pulmonary infiltration.



**Fig. 3** There are fine reticular infiltration in both lungs, mainly parahilar areas.



**Fig. 4** Chest radiograph shows coarse reticular infiltration in both lungs.



**Fig. 5.** Diffuse pulmonary infiltration with ground-glass appearance.

Associated abnormalities were minimal pleural effusion and cavity, presenting in 5 and 2 patients respectively.

There were 19 patients having documented concurrent extrapulmonary cryptococcal infection. Seventeen of these patients had cryptococcal meningitis with or without cryptococcal septicemia, lymphadenitis, hepatitis, urinary tract infection and skin infection. (Table. 3) Lumbar puncture was not performed in two patients who had only docu-

mented cryptococemia. In the remaining 3 patients extrapulmonary tissue was not sampled for evidence of cryptococcal infection. Four patients were diagnosed pulmonary cryptococcosis prior to meningitis.

Of the 18 patients receiving antifungal drugs, 12 patients improved, 1 patient initially improved but had been lost to follow-up and 5 patients died. All 4 patients who had not received antifungal treatment were dead.

**Table 2.** Summaries of radiographic appearances of pulmonary cryptococcosis

Diffuse infiltrates, predominantly interstitial pattern	14
- fine pattern (7)	
- intermediate pattern (5)	
- coarse pattern (2)	
Localized mixed infiltrates	6
Unilateral pleural effusion with equivocal infiltrate	1
mediastinal adenopathy alone	1
associated lesion	
pleural effusion	5
cavity	2



**Table. 3** Presence of extrapulmonary cryptococcal infection

	No. of cases
meningitis	8
meningitis + septicemia	4
meningitis + septicemia + lymphadenitis	2
meningitis + septicemia + hepatitis	1
meningitis + septicemia + nephritis + skin infection	1
meningitis + lymphadenitis	1
septicemia	2
no document	3

## DISCUSSION

*Cryptococcus neoformans* is a nonmycelial budding yeast found in a variety of environmental sites but most abundant in pigeon and chicken excreta. Lung is the portal of entry and in the normal host the organism could be irradiated by host defense mechanism, mainly cell mediated immunity (CMI).<sup>1</sup> In the immunocompromised host such as AIDS or immunosuppressed patients due to corticosteroid therapy, malignancy or immunosuppressive drugs, *C. neoformans* can significantly proliferate in the lungs and disseminate to other organs.<sup>4</sup>

Radiographic appearance of pulmonary cryptococcosis is found to be related to immunological competency.<sup>5</sup> In the study of Khoury et al revealed that immunocompetent hosts tended to have a single or multiple nodules but immunocompromised hosts demonstrated a wider variety of radiographic abnormalities including single or multiple nodules that progressed to confluence and/or cavitation, segmental consolidation, bilateral bronchopneumonia or a mixed pattern. Single or multiple nodules were the most common lesion followed by consolidation lesion. Adenopathy, cavitation and pleural effusion were limited to the immunocompromised hosts. However radiographic features of HIV-seronegative immunocompromised patients are quite different from HIV infected patients. Several series and this study

had found no large pulmonary nodule in AIDS patients with pulmonary cryptococcosis and interstitial infiltration had more frequently been reported, ranging from 57% to 80%.<sup>6-13</sup> So far, to our knowledge only one series of Chechani et al found large nodule (> 2 cm.) or circumscribed infiltration in 3 of 12 patients.<sup>11</sup> These figures may indicate more severity of immunosuppression in patients with AIDS and may reflect the inability to localize an infectious process to form large granulomatous nodules.

Two available series had described the patterns of interstitial infiltration which are more or less different from our series. Most of the patients in our series with diffuse interstitial infiltration had fine or intermediate patterns (12 in 14 patients) resembling pneumocystis carinii pneumonia and lesions in 4 of 12 patients could be described as ground-glass appearance. The coarse nodular infiltration were found in only 2 patients. In contrast, infiltration found in Miller et al series were predominantly nodular or coarse infiltration patterns and resembled advanced miliary TB in two patients.<sup>6</sup> Friedman et al also found predominantly coarse interstitial pattern in 9 of 14 patients and miliary nodules in one patient.<sup>8</sup> We postulate that the immunity in most of our AIDS patients may be more severely suppressed than those of the other two series causing less ability to form

such a coarse nodular infiltration. However our study is a retrospective form so the complete data of lymphocytic count could not be obtained and the number of patients in our study and other studies are too small to be statistically significant. Furthermore, the study of Friedman et al did not exclude cases with pulmonary copathogen, so comparison cannot be clearly made.

Cavities were associated lesion uncommonly found. Five series reported no obvious cavity<sup>6-9,12</sup> while 3 series found a small number of cavities; 2 in 17 patients,<sup>10</sup> 2 in 12 patients,<sup>11</sup> 1 in 3 patients respectively.<sup>13</sup> Our study found cavities in only 2 of 22 patients. Since in severely immunocompromised HIV-positive patients there is poor immune response to form granuloma and central necrosis, so cavities are less frequent.

Intrathoracic adenopathy was quite uncommon in our study being observed in only 1 out of 22 patients. The presence of adenopathy in each series varied from; 3 in 7 patients,<sup>6</sup> 4 in 5 patients,<sup>7</sup> 3 in 17 patients<sup>10</sup> and 1 in 10 patients.<sup>12</sup> These series had excluded all cases with pulmonary copathogen.

There are series of Chechani, Friedman and Mayohas which reported negative chest films; 3 in 12 patients, 2 in 14 patients and 1 in 17 patients respectively, suggesting endobronchial lesion or early infection. No negative chest film was noted in our study.

Even though signs and symptoms of pulmonary cryptococcosis were nonspecific such as fever, cough and headache we noted that most of the patients had concurrent extrapulmonary cryptococcal infection particularly meningitis similar to that of the others.<sup>6,8,10,11,13</sup> Although the study of Wasser et al had focused on primary pulmonary cryptococcosis, soon after, all patients did develop cryptococcal meningitis.<sup>7</sup> These confirm that the nature of pulmonary cryptococcosis in immunocompromised host is a disseminated

disease and pulmonary cryptococcosis alone may be unusual.

Occasionally, pulmonary cryptococcosis could be an initial presentation of cryptococcal infection or diagnosed prior to the diagnosis of cryptococcal meningitis as depicted by our study (4 in 20 patients), Wasser et al (5 in 20 patients),<sup>7</sup> Kovacs et al (3 in 27 patients),<sup>14</sup> Zuger et al (4 in 26 patients)<sup>15</sup> and Chuck et al (4 in 106 patients).<sup>16</sup> Recent reports had suggested that more than half of the patients have primary cryptococcal pneumonia.<sup>9,17</sup>

The treatment outcome was quite good as there were 12 from 16 patients improved following antifungal drug administration, whereas 4 patients who did not receive any specific treatment died. So, precised and early diagnosis is very important in order to decrease mortality rate.

In conclusion, pulmonary cryptococcosis in AIDS patients is becoming a more frequent opportunistic infection and usually has concurrent extrapulmonary cryptococcosis, particularly meningitis. Occasionally it is the initial presentation. Clinical features are nonspecific such as fever, cough and headache. Radiographic appearances were mostly diffusely mixed infiltration, predominantly fine or intermediate interstitial pattern, resembling pneumocystis carinii pneumonia. Localized infiltration are less frequent. Small pleural effusion, mediastinal adenopathy and cavities are evident in some cases. Pulmonary cryptococcosis should be considered in AIDS patients than ever before and the sooner the diagnosis is made the better therapeutic outcome can be expected.

## REFERENCES

1. Murray JF, Mills J. Pulmonary infectious complications of human immunodeficiency virus infection. *Am Rev Respir Dis* 1990;141:1582-98



2. Prasest P, Peerapatanapokin V, Tharnphornpilas P, et al. Opportunistic infection and AIDS related conditions among AIDS/ARC cases in Thailand. *Thai AIDS Journal* 1993;5:181-7
3. Grant IH, Armstrong D. Fungal infections in AIDS. Cryptococcosis. *Infect Dis Clin North Am* 1988;2:457-64
4. Fraser RG, Pare JAP. *Diagnosis of disease of the chest.* Philadelphia Saunders, 1989: 975-85
5. Khoury MB, Godwin JD, Ravin CE, Gallis HA, Halvorsen RA, Putman CE. Thoracic cryptococcosis : immunologic competence and radiologic appearance. *AJR* 1984; 141:893-6
6. Miller WT Jr, Edelman JM, Miller WT. Cryptococcal pulmonary infection in patients with AIDS : radiographic appearance. *Radiology* 1990;175:725-8
7. Wasser L , Talavera W. Pulmonary cryptococcosis in AIDS. *Chest* 1987;92:692-5
8. Friedman EP, Miller RF, Severn A, Williams IG, Shaw PJ. Cryptococcal pneumonia in patients with the acquired immunodeficiency syndrome. *Clin Radiol* 1995;50:756 -60
9. Batungwanayo J, Taelman H, Bogaerts J. Pulmonary cryptococcosis associate with HIV-1 infection in Rwanda:a retrospective study of 37 cases. *AIDS* 1994;8:1271-6
10. Meyohas MC, Roux P, Bollens D, et al. Pulmonary cryptococcosis localized and disseminated infections in 24 patients with AIDS. *Clin Infect Dis* 1995;21:625-33
11. Chechani V, Kamholz SL. Pulmonary manifestation of disseminated cryptococcosis in patients with AIDS. *Chest* 1990;98:1060-6
12. Sider L, Wescott MA. Pulmonary manifestation of cryptococcosis in patients with AIDS : CT features. *J thoracic imaging* 1994;9:78-84
13. Martos A, Mascoro J, Santin M, et al. Pulmonary cryptococcosis in AIDS. *Enfermedades infeccion y Microbiologia clinica* 1992;10:607-10
14. Kovacs JA, Kovacs AA, Polis M , et al. Cryptococcosis in the acquired immunodeficiency syndrome. *Ann Intern Med* 1985;103:533-8
15. Zuger A, Louie E, Holzman RS, Simberkoff MS, Rahal JJ. Cryptococcal disease in patients with acquired immunodeficiency syndrome. *Ann Intern Med* 1986;104:234-40
16. Chuck SL, Sande MA. Infections with cryptococcal neoformans in acquired immunodeficiency syndromes. *New Eng J Med* 1989;12 :794-9
17. Clerk RA, Greer DL, Valainis GT, et al. Cryptococcal neoformans pulmonary infection in HIV-1- infected patients. *J acquir immune Defic Syndr* 1990;3:480-4